

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 25 JUL 2005

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Applicant's or agent's file reference B03-0567PC		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2004/008497		International filing date (day/month/year) 29.07.2004	Priority date (day/month/year) 31.07.2003	
International Patent Classification (IPC) or national classification and IPC C07F9/50				
Applicant BASF AKTIENGESELLSCHAFT et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 3 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in Item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 20.04.2005		Date of completion of this report 22.07.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Richter, H Telephone No. +49 89 2399-8539		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/008497

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-9 received on 20.04.2005 with letter of 20.04.2005

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
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International application No.
PCT/EP2004/008497

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-9
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-9
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following documents:

D1 = WO-A-00/32612

D2 = US-A- 5321148

D3 = US-A-5276219

D4 = US-A-5912378

D5 = GB-A-2280671

The document D1 is regarded as being the closest prior art to the subject-matter of claim and discloses (the references in parentheses applying to this document):

A process for the preparation of acyl phosphines of formula I (claim 1), wherein n is 1 (claims 5, 10)

R1 is

C1-C18-alkyl, C2-C18-alkyl which is interrupted by one or several non-successive O atoms; phenyl-substituted C1-C4-alkyl, C2-C8-alkenyl, phenyl, naphthyl, biphenyl, C5-C12-cycloalkyl or a 5-or 6-membered O-, S-or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl, C5-C12-cycloalkyl or the 5-or 6-membered O-, S-or N-containing heterocyclic ring being unsubstituted or substituted by one to five halogen, C1-C8-alkyl, C1-C8-alkylthio and/or C1-C8-alkoxy;

R2 is C1-C18-alkyl, C3-C12-cycloalkyl, C2-C8-alkenyl, phenyl, naphthyl, biphenyl or a 5-or 6 membered O-, S-or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl or 5-or 6-membered O-, S-or N-containing heterocyclic ring being unsubstituted or substituted by one to four C1-C8-alkyl, C1-C8-alkoxy, C1-C8-alkylthio and/or halogen;

R3 is C1-C18-alkyl, C2-C18-alkyl which is interrupted by one or several non-successive O atoms; phenyl-substituted C1-C4-alkyl, C2-C8-alkenyl, phenyl, naphthyl, biphenyl, C5-C12-cycloalkyl or a 5-or 6-membered O-, S-or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl, C5-C12-cycloalkyl or the 5-or 6-membered O-, S-or N-containing heterocyclic ring being unsubstituted or substituted by one to five halogen,

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C1-C8-alkyl,
C1-C8-alkylthio and/or C1-C8-alkoxy;
by (1) reacting organic phosphorus halides of formula (II)
wherein R1, R3, and m have the meaning cited above,
and Y is Br or Cl,
with an alkali metal or with magnesium in combination with lithium, or with mixtures
thereof, in the presence of a catalyst (claim 10),
and (2) subsequent reaction with m acid halides of formula (III)
wherein R2, Y and m have the meaning cited above; which process is carried out without
isolation of the intermediates.

A process (claim 3) according to either claim 1 or claim 2, wherein
R1 is C1-C12-alkyl, cyclohexyl, phenyl or biphenyl, the radicals phenyl and biphenyl being
unsubstituted or substituted by one to four C1-C8-alkyl and/or C1-C8-alkoxy;
R3 is C1-C12-alkyl, cyclohexyl, phenyl or biphenyl, the radicals phenyl and biphenyl being
unsubstituted or substituted by one to four C1-C8-alkyl and/or C1-C8alkoxy;

A process (claim 4) according to either claim 1 or claim 2, wherein
R2 is phenyl which is substituted in 2,6- or 2,4,6-position by C1-C4alkyl and/or C-C4-
alkoxy.

A process (claim 6) according to either claim 1 or claim 2, wherein Y in formula (II) is
chloro.

A process (claim 7) according to either claim 1 or claim 2, wherein the reaction (I) is carried
out using lithium, **sodium** or potassium.

A process (claim 8) according to claim 7, wherein from 4 to 6 atom equivalents of the alkali
metal are used for the preparation of compounds of formula 1, wherein m is 2, and 2 to 3
atom equivalents of the alkali metal are used for the preparation of compounds of formula
1, wherein m is 1.

A process (claim 9) according to either claim 1 or claim 2, wherein Y in the compounds of
formula III is chloro.

A process (claim 11) according to either claim 1 or claim 2, which comprises carrying out

the reaction (1) of the organic phosphorus halides (II) with an alkali metal in the temperature range from -20 to +120°C

A process (claim 13) according to either claim 1 or claim 2, wherein the reaction (2) of the metallised phosphine with the acid chloride (III) is carried out at -20 to +80°C.

A process (claim 14) according to either claim 1 or claim 2, wherein the reaction steps (1) and (2) are carried out in the same solvent, preferably in tetrahydrofuran.

The catalyst according to D1 (see page 8, paragraph 4) may be an aromatic hydrocarbon having heteroatoms. within this definition falls the activator chlorobenzene according to claim 4.

The subject-matter of claims 1-4 and 6-9, therefore, differs from this known D1 process only in that the alkali metal selected is sodium and is present in the form of a dispersion of alkali metal particles having a mean size of $\geq 500 \mu\text{m}$ in the solvent.

The process claim 5 additionally differs from this known D1 process in the use of a high speed stirrer. The features according to claims 5 and 6 belong to the common knowledge of the skilled person and can thus not be a reason for an inventive merit (high speed agitation, see D4, column 2, line 36; D2, column 2, line 13).

The problem to be solved by the present invention may therefore be regarded as making available a new process for preparing compounds of formula (I).

The solution proposed in claims 1-9 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

Sodium metal when used as a reagent is in the form of a dispersion of the metal in the solvent. The particle size is usually less than $500 \mu\text{m}$ in commercially available material as can be seen from the epodoc logfile printouts 32/32 of WO8706234 and 19/32 (US4987202). Other hits 3/32 and 7/32 -9/32 just like D5 show that a particle size of less than $500 \mu\text{m}$ is connected to the feature "sodium dispersion".

All the documents show that the selected particle size in claim 1 is virtually no limiting factor. No document has been found during the search in which the particle size of an

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International application No.

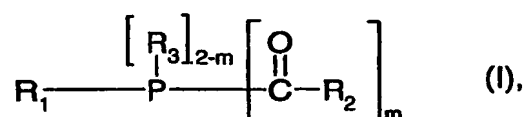
PCT/EP2004/008497

alkali metal in the dispersion is above the limit of present claim 1. Hence, the skilled person knows that a sodium dispersion in which the particle size is less than 500 μm is normally employed in chemical reactions.

Claims 1-9, therefore, lack inventive merit over the combination of D1 and the knowledge of the skilled person.

Claims

1. A process for the preparation of acylphosphines of formulä (I)



10 wherein

m is 1 or 2;

15 R_1 is C_1 - C_{18} alkyl, C_2 - C_{18} alkyl which is interrupted by one or several non-successive O atoms, phenyl substituted C_1 - C_4 alkyl, C_2 - C_8 alkenyl, phenyl, naphthyl, biphenyl, C_5 - C_{12} cycloalkyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl, C_5 - C_{12} cycloalkyl or the 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to five halogen, C_1 - C_8 alkyl, C_1 - C_8 alkylthio and/or C_1 - C_8 alkoxy;

20 R_2 is C_1 - C_{18} alkyl, C_3 - C_{12} cycloalkyl, C_2 - C_{18} alkenyl, phenyl, naphthyl, biphenyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl or 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to four C_1 - C_8 alkyl, C_1 - C_8 alkoxy, C_1 - C_8 alkylthio and/or halogen;

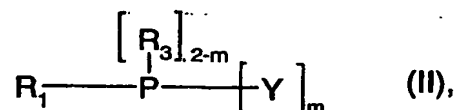
25 R_3 is C_1 - C_{18} alkyl, C_2 - C_{18} alkyl which is interrupted by one or several non-successive O atoms; phenyl substituted C_1 - C_4 alkyl, C_2 - C_8 alkenyl, phenyl, naphthyl, biphenyl, C_5 - C_{12} cycloalkyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl, C_5 - C_{12} cycloalkyl or the 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to five halogen, C_1 - C_{18} alkyl, C_1 - C_8 alkylthio and/or C_1 - C_8 alkoxy;

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by

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(1) reacting organic phosphorus halides of formula (II)



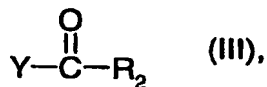
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wherein R_1 , R_3 and m have the meaning cited above;
and Y is Br or Cl,

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with sodium in a solvent in the presence of an activator, wherein sodium is present in the form of a dispersion of sodium particles having a mean particle size of $\leq 500 \mu m$ in the solvent,

(2) subsequent reaction with acid halides of formula (III)



15

wherein R_2 and Y have the meaning cited above;
which process is carried out without isolation of the intermediates.

- 20 2. The process according to claim 1, wherein R_1 , R_2 and R_3 are independently from each other phenyl, naphthyl and biphenyl, being unsubstituted or substituted by one to five halogen, C_1 - C_8 alkyl and/or C_1 - C_8 alkoxy.
- 25 3. The process according to claim 2, wherein R_1 and R_3 are phenyl and R_2 is 2,4,6-trimethylphenyl.
4. The process according to any one of claims 1 to 3, wherein the activator is chlorobenzene and/or n-butanol.
- 30 5. The process according to any one of claims 1 to 4, wherein the alkali metal is dispersed in the solvent by means of a high speed turbine stirrer.
- 35 6. A process according to any one of claims 1 to 5, wherein from 4 to 8 atom equivalents of the alkali metal are used for the preparation of compounds of formula (I), wherein m is 2, and 2 to 4 atom equivalents of the alkali metal are used for the preparation of compounds of formula (I), wherein m is 1.

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7. A process according to any one of claims 1 to 6, wherein the reaction (1) of the organic phosphorus halides (II) with an alkali metal is carried out in the temperature range from -20° to $+160^{\circ}\text{C}$.
8. A process according to any one of claims 1 to 7, wherein the reaction (2) of the metallised phosphine with the acid chloride (III) is carried out at -20° to $+120^{\circ}\text{C}$.
- 10 9. A process according to any one of claims 1 to 8, wherein the reaction steps (1) and (2) are carried out in toluene or ethyl benzene as solvent.